



213.1077-CRIM-1600/2900

UNITED STATES PATENT AND TRADEMARK OFFICE

Examiner: Unknown Art Unit: 1614
Re: Application of: CHOE, Y.H., et al.
 Serial No.: 10/078,730
 Filed: February 19, 2002
 For: **TERMINALLY-BRANCHED
POLYMERIC LINKERS AND
POLYMERIC CONJUGATES
CONTAINING THE SAME**

INFORMATION DISCLOSURE STATEMENT

Assistant Commissioner
for Patents
Washington, D.C. 20231

August 8, 2002

Sir:

Pursuant to M.P.E.P. §609 and 37 C.F.R. §§1.56, 1.97-1.99, Applicants herewith submit form PTO-1449 (7 sheets) which lists references of which Applicants are aware. The Examiner is also alerted to the fact that the following related patent applications are currently pending in the United States Patent and Trademark Office: United States Patent Application Serial Nos. 10/067,930, 09/852,335, 09/758,993 and 10/078,649.

This submission does not represent that a search has been made or that no better art exists. While the term "references" is used in citing the U.S. patents called to the Examiner's attention herein, Applicants do not make any admission that each or all of them are "prior art" references within the meaning of the statutory and case law.

Applicants reserve the right to contend, where appropriate, that a patent asserted against any claim of the present application is not prior art under the facts and the law.

Applicants also reserve the right to present appropriate arguments and/or evidence to establish patentability over the references, should one or more of the references be applied against the claims of the present application.

Applicants request that the Examiner independently determine those items which the Examiner would consider the most pertinent of all the references cited herein.

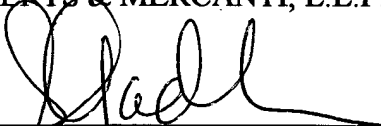
This Information Disclosure Statement is filed before the mailing date of a first Office Action on the merits. Accordingly, this document complies with the requirements of 37 C.F.R. §1.97(b).

No fee is believed to be due. Any deficiency or overpayment concerning this document should be charged or credited to Deposit Account No. 50-0217. A duplicate copy of this sheet is enclosed.

It is respectfully requested that the references cited in the accompanying PTO-1449 Form be considered and made of record.

Respectfully submitted,

ROBERTS & MERCANTI, L.L.P.



Sapna Gadhia
Reg. No. 48,978

ROBERTS & MERCANTI, L.L.P.
P.O. Box 3156
105 Lock Street, Suite 203
Newark, New Jersey 07103-0156
Phone: 973-621-0660
Fax: 973-621-0774

J:\ENZON\1070-1079\1077\CRNL2-UNDS.wpd

I hereby certify that this correspondence and/or fee is being deposited with the United States Postal Service as first class mail in an envelope addressed to "Assistant Commissioner of Patents, Washington, D.C. 20231" on August 8, 2002.
ROBERTS & MERCANTI, L.L.P.

BY:



Sapna Gadhia

INFORMATION DISCLOSURE CITATION

(Use several sheets if necessary)

ATTY DOCKET NO.

213.1077-CRNL-U

SERIAL NO.

1078,730

Choe, Y. H., et al.

FILING

02/19/2002

GROUP

U.S. PATENT DOCUMENTS

*EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
	A1	5,965,119	10/12/99	Greenwald, et al.			12/30/97
	A2	5,130,126	07/14/92	Koyama, et al.			03/28/91
	A3	5,994,517	11/30/99	Ts'o, et al.			11/22/96
	A4	6,039,931	03/21/00	Schmitt-Willich, et al.			10/06/94
	A5	6,020,373	02/01/00	Schellenberg, et al.			04/21/97
	A6	5,885,548	03/23/99	Maier, et al.			11/30/95
	A7	5,756,825	05/26/98	Safavy, et al.			04/16/93
	A8	4,943,579	07/24/90	Vishnuvajjala, et al.			10/06/87
	A9	5,283,339	02/01/94	Arnold, et al.			08/05/92
	A10	5,433,886	07/18/95	Sherbondy, et al.			05/07/92
	A11	5,643,575	07/01/97	Martinez, et al.			10/27/93

FOREIGN PATENT DOCUMENTS

		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION	
							YES	NO
	A12	WO 99/45964	09/16/99	PCT				
	A13	WO 96/23794	08/08/96	PCT				
	A14	WO 81/01145	04/30/81	PCT				
	A15	WO 93/24476	12/09/93	PCT				
	A16	WO 95/10304	04/20/95	PCT				

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

	A17	Guiotto, Andrea, et al., An Improved Procedure for the Synthesis of Branched Polyethylene Glycols (PEGs) with the Reporter Dipeptide Met-Beta-Ala for Protein Conjugation, Bioorganic & Medicinal Chemistry Letters, volume 12, pgs. 177-180 (2002).
	A18	Ranganathan, D., et al. Synthesis of Totally Chiral, Multiple Armed, Poly Glu and Poly Asp Scaffoldings on Bifunctional Adamantane Core, Tetrahedron Letters, Volume 38, Number 7, p. 1265-68 (1997).

EXAMINER

DATE CONSIDERED

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

INFORMATION DISCLOSURE CITATION

(Use several sheets if necessary)

ATTY DOCKET NO.

213.1077-CRNL-U

SERIAL NO.

10/078,730

Choe, Y. H., et al.

FILING

02/19/2002

GROUP

161

U.S. PATENT DOCUMENTS

*EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
	A19	5,646,159	07/08/97	Wall, et al.			07/20/94
	A20	5,679,852	10/21/97	Platzek, et al.			06/02/95
	A21	5,583,206	12/10/96	Snow, et al.			11/28/94
	A22	5,693,310	12/02/97	Gries, et al.			11/19/90
	A23	5,454,954	10/03/95	Alfano, et al.			11/02/94
	A24	5,569,720	10/29/96	Mongelli, et al.			07/27/95
	A25	5,547,981	08/20/96	Greenwald, et al.			02/17/94
	A26	5,622,986	04/22/97	Greenwald, et al.			10/19/94
	A27	4,179,337	12/18/79	Davis, et al.			07/28/77
	A28	5,183,660	02/02/93	Ikeda, et al.			08/15/91
	A29	5,489,589	02/06/96	Wittman, et al.			12/07/94

FOREIGN PATENT DOCUMENTS

		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION	
							YES	NO
	A30	WO 98/13059	04/02/98	PCT				
	A31	WO 01/09139 A1	02/08/01	PCT				
	A32	WO 96/22277	07/25/96	PCT				
	A33	WO 99/30727	06/24/99	PCT				

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

	A34	Twyman, L.J., et al., The Synthesis of Water Soluble Dendrimers, and their Application as Possible Drug Delivery Systems, Tetrahedron Letters, Volume 40, p. 1743-46 (1999).
	A35	Greenwald, R.B., Review Oncologic, Endocrine & Metabolic Drug Delivery Systems: anticancer prodrugs and their polymeric conjugates. Exp. Opin. Ther. Patents (1997) 7(6): 601-609

EXAMINER

DATE CONSIDERED

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

INFORMATION DISCLOSURE CITATION

(Use several sheets if necessary)

ATTY DOCKET NO.
213.1077-CRNL-U

SERIAL NO.
1078,730

Choe, Y. H., et al.

FILING
02/19/2002

GROUP
1614

U.S. PATENT DOCUMENTS

*EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
	A36	5,498,729	03/12/96	Domb			02/22/93
	A37	5,614,549	03/25/97	Greenwald, et al.			01/30/95
	A38	5,672,584	09/30/97	Borchardt, et al.			04/25/95
	A39	6,113,906	09/05/00	Greenwald, et al.			12/29/98
	A40	5,605,976	02/25/97	Martinez, et al.			05/15/95
	A41	5,561,119	10/01/96	Jacquesy, et al.			04/29/92
	A42	5,349,001	09/20/94	Greenwald, et al.			01/19/93
	A43	5,321,095	06/14/94	Greenwald			02/02/93
	A44	5,122,614	06/16/92	Zalipsky			04/19/90
	A45	5,093,531	03/03/92	Sano, et al.			05/05/89
	A46	4,179,337	12/18/79	Davis, et al.			07/28/77

FOREIGN PATENT DOCUMENTS

		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION	
							YES	NO

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

	A47	Cerny, L. C., et al., A Potential Blood Substituted from A Tetronic Polyol And A Modified Hemoglobin, Art. Cells & Immob. Biotech., 20(1), 71-93 (1992)
	A48	Ohya, Y., et al., Synthesis and Cytotoxic Activity of Conjugates of Monomethoxy-Poly-(ethylene glycol) End- Capped with Doxorubicin via Ester, Amide, or Schiff's Base Bond, Journal of Bioactive and Compatible Polymers Vol. 10 Jan., 1995, 51-66

EXAMINER

DATE CONSIDERED

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

INFORMATION DISCLOSURE CITATION

(Use several sheets if necessary)

ATTY DOCKET NO.
213.1077-CTML-U

SERIAL NO.
1678,730

Choe, Y. H., et al.

FILING
02/19/2002

GROUP
1614

U.S. PATENT DOCUMENTS

*EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
	A49	5,112,739	05/12/92	Meneghini, et al.			08/02/88
	A50	5,710,135	01/20/98	Leenders, et al.			05/24/96
	A51	5,382,657	01/17/95	Karasiewicz, et al.			08/26/92
	A52	5,614,549	03/25/97	Greenwald, et al.			01/30/95
	A53	5,840,900	11/24/98	Greenwald, et al.			08/20/96
	A54	6,005,002	12/21/99	Springer, et al.			01/19/96

FOREIGN PATENT DOCUMENTS

		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION	
							YES	NO

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

	A55	Shearwater Polymers, Inc., Catalog Polyethylene Glycol Derivatives, 1997-1998
	A56	Williams, Matthew A., and Henry Rapoport, Synthesis of Enantiomerically Pure Diethylenetriaminepentaacetic Acid Analogues, J. Org. Chem. 1193, 58, 1151-1158

EXAMINER

DATE CONSIDERED

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

INFORMATION DISCLOSURE CITATION <i>(Use several sheets if necessary)</i>		Docket Number (Optional) 213.1077-CRNL-U	Application Number 10/078,730
		Applicant(s) Choe, Y.H., et al.	
		Filing Date 02/19/2002	Group Art Unit 1614

*EXAMINER INITIAL	OTHER DOCUMENTS	(Including Author, Title, Date, Pertinent Pages, Etc.)
A57		Zalipsky, S., C. Gilon and A. Zilkha, Attachment of Drugs to Polyethylene Glycols, <i>Eur. Polym. J.</i> , Vol. 19, No. 12, pp. 1177-1183, 1983
A58		Shearwater Polymers, Inc., Quarterly Newsletter, March 1998
A59		Ouchi, T., et al., Synthesis and Antitumor Activity of Poly(Ethylene Glycol)s Linked to 5-Fluorouracil via a Urethane or Urea Bond. <i>Drug Design & Discovery</i> , 1992, Vol. 9, pp. 93-105
A60		Greenwald, Richard B., et al., Drug Delivery Systems Employing 1,4-or 1,6-Elimination: Poly(ethylene-glycol) Prodrugs of Amine-Containing Compounds, <i>Journal of Medicinal Chemistry</i> , Volume 42, Number 18, pages 3657-3667, 1999
A61		Maeda H., et al., Tumor vascular permeability and the EPR effect in macromolecular therapeutics: a review, <i>Jour. of Controlled Release</i> 65 (2000) pages 271-284
A62	✓	Greenwald, Richard B., et al., Drug Delivery Systems Based on Trimethyl Lock Lactonization: Poly(ethylene glycol) Prodrug of Amino-Containing Compounds, <i>Journal of Medicinal Chemistry</i> , Volume 43, Number 3, pages 475-487 (2000)
A63	✓	de Bont, Dries B.A., et al., Synthesis and Biological Activity of B-Glucuronyl Carbamate-Based Prodrugs of Paclitaxel as Potential Candidates for ADEPT, <i>Bioorganic & Medicinal Chemistry</i> , Volume 5, Number 2, pages 405-414 (1997)
A64	✓	Shearwater Polymers, Inc., Catalog- Polyethylene Glycol Derivatives, Star PEGS and Branched PEGS & Sulfhydryl Selective PEGS, 1997-1998; p.8,33
A65	✓	Leenders, R.G.G., et al., Highly Diastereoselective Synthesis of Anomeric B-O-Glycopyranosyl Carbamates from Isocyanates, <i>Synthesis</i> , November 1996; pp 1309-1312
A66	✓	Leenders, R.G.G., et al., B-Gucuronyl Carbamate Based Pro-moieties Designed for Prodrugs in ADEPT, <i>Tetrahedron Letters</i> Vol. 36, No. 10 pp. 1701-1704 (1995)
A67		Waldmann, H., et al., Synthesis of the Palmitoylated and Farnesylated C-Terminal Lipoheptapeptide of the Human N-Ras Protein by Employing an Enzymatically Removable Urethane Protecting Group, <i>Angew. Chem Int. Ed.</i> 1995, 34, No.20, pp. 2259-2262
A68	✓	Jungheim, L.N. et al., Design of Antitumor Prodrugs: Substrates for Antibody Targeted Enzymes, <i>Chem. Rev.</i> 1994, Volume 94, pp. 1553-1566

EXAMINER	DATE CONSIDERED

*EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP Section 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

INFORMATION DISCLOSURE CITATION

(Use several sheets if necessary)

Docket Number (Optional)

213.1077-CRNL-U

Application Number

107878,730

Applicant(s)

Choe, Y.H., et al.

Filing Date

02/19/2002

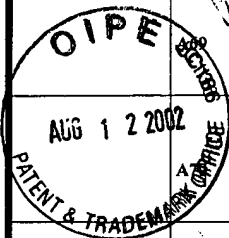
Group Art Unit

16

RECEIVED
AUG 1 2002
TECH CENTER 1600/2900

*EXAMINER
INITIAL

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)



- | | |
|-----|---|
| | Bundgaard, H., The Double Prodrug Concept and its Applications, Advanced Drug Delivery Reviews, Vol. 3, pp. 39-65 (1988) |
| | Wakselman, M. et al., An Alkali-labile Substituted Benzyloxycarbonyl Amino-protecting Group, JCS Chem. Comm. pp. 593-594 (1973) |
| A71 | Cari, P.L., et al., A Novel Connector Linkage Applicable in Prodrug Design, J. Med. Chem., Vol. 24, No. 5, 479-480 (1981) |
| A72 | Wang, B., et al., Synthesis of a Novel Esterase-Sensitive Cyclic Prodrug System for Peptides That Utilizes a "Trimethyl Lock" Facilitated Lactonization Reaction, J. Org. Chem (1997), 62, 1363-67 |
| A73 | Amsberry, K.L. et al., The Lactonization of 2'-Hydroxyhydrocinnamic Acid Amides: A Potential Prodrug for Amines, J. Org. Chem. Vol. 54, No. 23, pp. 5867-5877 (1998) |
| A74 | Carpino, L.A., Reductive Lactonization of Strategically Methylated Quinone Propionic Acid Esters Amides, J. Org. Chem., Vol. 54, No. 14, pp. 3303-3310 (1989) |
| A75 | Wang, B., et al., Chemical Feasibility Studies of a Potential Coumarin-Based Prodrug System, Bioorganic & Medicinal Chemistry Letters, Vol. 6, No. 8, pp 945-50 (1996) |
| A76 | Wang, et al., Coumarin-based Prodrugs 2. Synthesis and Bioreversibility Studies of an Esterase-Sensitive Cyclic Prodrug of Dadle, an Opioid Peptide, Bioorg. & Med. Chem. Letters, Vol. 6, No. 23, 2823-26 (1996) |
| A77 | Amsberry, K., et al., Amine Prodrugs which Utilize Hydroxy Amide Lactonization. I.A. potential Esterase-Sensitive Amide Prodrug Pharmaceutical Research Vol. 8, No. 4, 1991 |
| A78 | Shan, D., et al., Prodrug Strategies Based on Intramolecular Cyclization Reactions, Journal of Pharmaceutical Sciences, July 1997, Vol. 86, No. 7, pp 765-767 |
| A79 | Brana, Miguel, et al., Synthesis of Antitumor Dendritic Imides, Bioorganic & Medicinal Letters 11 (2001) Pgs. 3027-3029 |
| A80 | Bogdanov, et al. Long-Circulating Blood Pool Imaging Agents, Advanced Drug Delivery Reviews 16 (1995) p. 335-348 |

EXAMINER

DATE CONSIDERED

*EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP Section 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

INFORMATION DISCLOSURE CITATION

(Use several sheets if necessary)

Docket Number (Optional)

213.1077-CRNL-U

Application Number

10/078 730

Applicant(s)

Choe, Y.H., et al.

Filing Date

02/19/2002

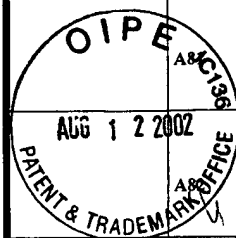
Group Art Unit

1614

RECEIVED
AUG 14 2002
TECH CENTER 16012900

*EXAMINER
INITIAL

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)



Hermentin, et al., Attachemnt of Rhodosaminylanthracyclinone-Type Anthracyclines to the Hinge Region of Monoclonal Antibodies, Bioconjugate Chem., Vol. 1, No. 2, p. 100-107 (1990)

Zier, et al., Polyethylene Glycol Bound Benzyl and Flourenyl Derivatives as Solubilizing Side-Chain Protecting Groups in Peptide Synthesis, Tetrahedron Letters, Volume 35, No. 7., pages 1039-1042 (1994)

Greenwald, et al., Poly(ethylene glycol) Conjugated Drugs and Prodrugs: A Comprehensive Review, Critical Reviews in Therapeutic DDrug Carrier Systems, 17(2): 101-161 (2000)

Hines, Jennifer V., et al., Paramagnetic Oligonucleotides: Contrast Agents for Magnetic Resonance Imaging with Proton Relaxation Enhancement Effects. ,Bioconjugate Chem., Vol. 10, No. 2, 1999, pp 155-158.

Chen, Jiyan., Thiol-Reactive Luminescent Chelates of Terbium and Europium, Bioconjugate Chem. 1999, 10, 311-315.

King, Dalton H., et al., Monoclonal Antibody Conjugates of Doxorubicin Prepared with Branched Linkers: A Novel Method for Increasing the Potency of Doxorubicin Immunoconjugates., Bioconjugate Chem., Vol. 10, pp 279-288 (1999)

Greenwald, R.B., et al., Highly Water Soluble Taxol Derivatives 2'-Polyethyleneglycol Esters As Potential Prodrugs, Bioorganic & Medicinal Chemistry Letters, Vol 4. No. 20, pp. 2465-2470 (1999)

Ueda, Y., et al., Synthesis and Antitumor Evaluation of 2'-Oxcarbonylpaclitaxels (Paclitaxel-2'-Carbonates) Bioorganic & Medicinal Chemistry Letters, Vol. 4, No. 15., pp. 1861-1864 (1994)

Greenwald, et al., Drug Delivery Systems based on Trimethyl Lock Lactonization: Poly(ethylene glycol) Prodrugs of amino-containing compounds; 2000, Chem. Abstract 132: 227266

Greenwald, et al., Trialkyl-Lock-Facilitated Polymeric Prodrugs of Amino-containing Bioactive Agents; 1999, Chem. Abstract 131: 92540

EXAMINER

DATE CONSIDERED

*EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP Section 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.